National Pork Board

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March 31, 2003

Chief, Standardization Branch
Livestock and Seed Program
AMS, USDA, Room 2603-S, Stop 0254
1400 Independence Avenue SW
Washington, DC 20250-0254

Re: Docket No. LS-02-02; United States Standards for Livestock and Meat Marketing Claims

These comments are submitted on behalf of the National Pork Board in response to your request for comments. The National Pork Board was established by an act of Congress in 1985 and is responsible for the collection, distribution, and program accountability for the money generated by the pork checkoff. A Board led by 15 pork producers creates programs in the areas of promotion, research, and consumer information. These programs support producers by providing them with information on many areas including swine health and pork safety. The information contained in this communication is intended to share scientific information and experiences generated by producer checkoff investments and the application of that information to pork production.

The National Pork Board appreciates this opportunity to provide technical comments on the proposed Standards for Livestock and Meat Marketing Claims. It is important that these claims are technically correct, and at the same time are clear to consumers. Has the Agricultural Marketing Service (AMS) conducted focus groups with consumers to determine their understanding of the proposed label claims or alternative language? We are providing comments on the Antibiotic, Hormone and Product Characteristics Claims.

Claims Relating to Live Animal Production – Antibiotic Claims

1. **"No antibiotics used, or Raised without antibiotics."** A definition of antibiotics needs to be established for the purposes of this document. While the terms antibiotic and antimicrobial are often used interchangeably, the strict definition of an antibiotic is for a natural substance. There are antimicrobials used in animal agriculture that are not antibiotics. It is likely that consumers would believe that meat labeled "Raised without antibiotics" would be raised without antimicrobials as well, however, as written, technically the use of antimicrobials may be permitted.

2. **"No subtherapeutic antibiotics added, or Not fed antibiotics."** If the term subtherapeutic is to be used on a label, a definition of subtherapeutic needs to be established for the purposes of this rule. The Food and Drug Administration (FDA) defines therapeutic uses of antimicrobials as treatment, control and prevention of bacterial disease.[1] However, there is no well-accepted definition of subtherapeutic uses of antimicrobials.

[1] Judicious Use of Antimicrobials for Pork Producers, August 2001, Department of Health and Human Services, Public Health Service, Food and Drug Administration, Center for Veterinary Medicine. P. 10.

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The statement "no subtherapeutic antibiotics added" could be confusing to consumers. It could indicate that antibiotics were not added to the meat post-harvest rather than to an animal's diet.

Additionally, the claim "not fed antibiotics" appears to indicate that all antimicrobials administered in feed are subtherapeutic. There are numerous antimicrobials that are used to treat, control, or prevent bacterial disease through feed administration. It is not technically correct to treat these descriptions as interchangeable.

3. **"No detectable antibiotic residue (analyzed by 'method x')."** FDA has a rigorous, science-based approach to the licensing of New Animal Drugs. The approval process addresses not only the safety of the drug for use in the animal, but also the safety of meat consumed from animals that have received the drug. An overview, written by Dr. Mike Apley, on the FDA process for determining withdrawal times is attached[2]. It is not clear on what scientific basis "at least 30 days beyond the minimum FDA withdrawal requirement" was selected. While consumers may believe there is an indication of "additional" safety, FDA has already addressed the safety of antibiotic residues related to the product usage.

   This label claim may be misleading, as the limit of detection is not zero in any tests. While the claim does say "no detectable" the average consumer may construe that to mean this meat came from animals that had never received antimicrobials. In addition, will AMS set minimum standards for the analytical methods used for this claim? Who will be reviewing the testing protocol? It is conceivable that an analytical method could be used that is inferior to those used by FDA and the Food Safety and Inspection Service (FSIS), so that a product could have a violative residue but carry a "no detectable antibiotic residue" claim. Will AMS require method x to be at least as sensitive as the current FDA/FSIS methods? In addition, will all antibiotics used at any point in the production cycle of the animal need to be tested for?

Claims Relating to Live Animal Production - Hormone Claims

1. **"The terms 'hormone,' 'growth promotant,' 'growth stimulant' and 'implant' are used interchangeably."** Technically, for pork production, the terms are not interchangeable. The term growth promotant is commonly applied to use in the feed of low level applications of antimicrobials to enhance nutrient utilization. By using these terms interchangeably, the consumer could equate a "no growth promotant" claim to mean that the pig was fed no antimicrobials rather than administered no hormones.

   In the case of pork, it could also be misleading to allow any label claim related to hormones as no supplemental production hormones or implants are approved by FDA for use in market swine in the United States. It would seem appropriate to define these terms individually if they are to be used on label claims.

Claims Relating to Product (Meat) Characteristics

1. **"Company X's" Tender 'Species" – a tenderness management system must include at least 3 of the following controlled elements...** Many of the controlled elements listed, such as age or electrical stimulation, are really pertinent to beef rather than pork. How would AMS handle such a claim if an annual verification establishes that the product meets the threshold for tenderness, but does not meet three of the eight attributes listed? It is unclear why the attributes listed need to be included if the objective measurements of tenderness are satisfactory.

Summary

The National Pork Board appreciates this opportunity to comment on these proposed standards. By developing accurate definitions, achievable and consistent standards, backed up by AMS verification, pork producers will have new opportunities to differentiate their products in a meaningful manner in the marketplace.

Sincerely,

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Drug Residue Avoidance[2]

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How are withdrawal times determined for approved drugs?

The Food and Drug Administration's Center for Veterinary Medicine (FDA/CVM) provides guidance to the industry concerning drug approval requirements through guidance documents. Guideline number 3, General Principles For Evaluating The Safety Of Compounds Used In Food-Producing Animals, is the entry document for linking to more specific guidelines on the CVM website.[1] The introductory portion of this guideline is reproduced below.

> "The sponsor of the compound is required to furnish to FDA the scientific data necessary for demonstrating that the residues of the sponsored compound in the edible products of treated animals are safe. FDA has developed a series of guidelines to inform sponsors of the scientific data that FDA believes will provide an acceptable basis for determining the safety of the compound. The individual guidelines are listed below.
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> I. Guideline For Metabolism Studies And For Selection Of Residues For Toxicological Testing
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> II. Guideline For Toxicological Testing
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> III. Guideline For Threshold Assessment
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> IV. Guideline For Establishing A Tolerance *Changed To* Guideline For Establishing A Safe Concentration
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> V. Guideline For Approval Of A Method Of Analysis For Residues
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> VI. Guideline For Establishing A Withdrawal Period
>
> VII. Guideline For New Animal Drugs And Food Additives Derived From A Fermentation
>
> VIII. Guideline For The Human Food Safety Evaluation Of Bound Residues Derived From Carcinogenic New Animal Drugs
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> A guideline represents the agency's position on a procedure or practice at the time of its issuance. A guideline is not a legal requirement. A person may follow the guideline or may choose to follow alternate procedures or practices. If a person chooses to use alternate procedures or practices, that person may wish to discuss the matter further with FDA/CVM to prevent an expenditure of money and effort on activities that might later be determined to be unacceptable. The guideline does not bind the agency, and it does not create or confer any rights, privileges, immunities, or benefits for or on any person. When a guideline states a requirement imposed by statute or regulation, however, the requirement is law and its force and effect are not changed in any way by virtue of its inclusion in the guideline."

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[2] Excerpted from Proceedings, Pork Quality and Safety Summit. 2002. National Pork Board, Des Moines, IA.

While guidance is available in the form of these documents, companies pursuing approvals for new animal drugs will typically submit proposed study designs for review by the FDA/CVM prior to conducting the study. The procedures set forth in these documents are much more complicated than will be summarized in these proceedings. In short, the construction of a withdrawal time begins with data generated during toxicology tests (Part II) and the determination of an approved method of analysis (Part V). The toxicology data are used as a component of calculating an acceptable daily intake (ADI) and, subsequently, a safe concentration (Part IV). An excerpt from Part IV describes ADI determination.

> "As described in guideline II, the toxicology tests are designed to determine the dose at which the compound produces an adverse effect and a dose which produces no observed effect (NOEL). If the drug is not a carcinogen, the NOEL of the most sensitive effect in the most sensitive species divided by a safety factor is used to determine an acceptable daily intake (ADI) for drug residues. If the sponsor provides strong scientific data that this NOEL is not predictive of human toxicity, the FDA will use a more appropriate NOEL for establishing the ADI. Therefore, the ADI is calculated by dividing the NOEL obtained in the toxicology study with the most appropriate species by a safety factor."

The safe concentration in edible tissues is then calculated by using a formula involving the ADI (μg/kg/day), an average weight for a person (60 kg), and an estimated intake for edible tissues based on a standard table or scientifically justified values provided by the drug sponsor.. Along with metabolism data from the food-producing species determined using the approved analytical method, the safe concentrations can, in turn, be used to calculate tolerances for residues in the edible products (meat and/or milk and/or eggs) derived from treated animals. The Code of Federal Regulations contains "Specific Tolerances for Residues of New Animal Drugs". Values for approved drugs may be searched on line in 21CFR part 556 subpart B.[2] It is important to realize that if a drug is not approved for use in a species, then there are no tolerances for residues of that drug in the edible products derived from that species. When tolerances have not been established, the finding of any residue would be considered violative. Similar values in other countries may be referred to as Maximum Residue Limits (MRLs), although the specific calculation used to determine these values may differ from the methods used to establish tolerances.

The withdrawal time is calculated according to guidance issued in Part VI, with guidance for compounds classified as carcinogens contained in Part VIII. An excerpt from Part VI summarizes the statistical method for withdrawal time calculation.

> "This guideline describes a procedure for establishing a withdrawal period that is based on a statistical tolerance limit procedure (Ref. 1). The withdrawal period is determined when the tolerance limit on the residue concentration is at or below the permitted concentration. A tolerance limit provides an interval within which a given percentile of the population lies, with a given confidence that the interval does contain that percentile of the population. FDA will use the 99th percentile of the population and the 95 percent confidence level."

The withdrawal time is not just based on when the last animal in the study is below the established tolerance in the target tissue. It is based on statistical calculations for when residues in 99% of the animals will be below the established tolerance in the target tissue, and then the time is further extended to the outer limit (longest time) of a 95% confidence interval constructed around the 99% estimate using variation estimates derived from the study.

References

[1] Guideline No. 3, General Principles For Evaluating The Safety Of Compounds Used In Food-Producing Animals, Revised July 1994. U.S. Department Of Health And Human Services, Public Health Service, Food And Drug Administration, Center For Veterinary Medicine. Available at http://www.fda.gov/cvm/guidance/guideline3toc.html

[2] Code of Federal Regulations 21CFR556 subpart B, Specific Tolerances for Residues of New Animal Drugs, available on line at http://www.access.gpo.gov/nara/cfr/